

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

After amending the claims as set forth above, claims 1, 3, 10, 11, 16, 17, and 18-31 are now pending in this application.

Rejections under 35 USC 112, first paragraph

The Examiner rejected claims 1, 3, and 8-14 under 35 USC 112, first paragraph for allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicant respectfully traverses these rejections.

With respect to claims 1 and 3, Applicant points out that the claims are directed to methods for inducing apoptosis, and delivering a nucleic acid sequence, respectively. Thus, the citation of *Fiers v. Revel* and *Amgen v. Chugai* are inapposite, as the claims at issue in those cases were not method claims. In the present application, Applicant has described how to deliver thiaminases using conventional delivery methods or using bacterial vectors that encode and express the thiaminase. (In addition see application 09/113,596 and related PCT application PCT/US98/14496, which were incorporated by reference herein.) Further, Applicant has provided the sequences of two different thiaminases, *i.e.*, the *Naegleria gruberi* and *Bacillus thiaminolyticus* thiaminases. In addition, Applicant has identified a variety of other organisms from which thiaminases can be obtained. As a result, Applicant respectfully submits that no description is lacking for method claims 1 and 3.

With respect to claims 8-13, claims 8, 9, 12, and 13 were cancelled above. New claims 18 and 19 directed to nucleic acid sequences and claims 25-27 directed to bacteria that encode a thiaminase were submitted. Applicant respectfully submits that the present rejection is inapplicable to the present claims directed to nucleic acid sequences. Further, description of

bacteria encoding a recombinant thiaminase are sufficiently described by the indication of suitable bacteria, as one of ordinary skill in the art is familiar with insertion of selected recombinant sequences in such bacteria.

In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw the rejections under 35 USC 112, first paragraph.

Rejections under 35 USC 112, second paragraph - enablement

The Examiner rejected claims 1, 3, and 8-14 for allegedly lacking enablement, asserting that the claimed invention encompasses gene therapy. Applicant respectfully traverses these rejections as they may be considered in connection with the present claims.

Applicant requests that the Examiner note that the present claims do not concern transfection of human cells. Thus, the references cited by the Examiner are inapplicable to the present claims. Accordingly, Applicant requests that the Examiner reconsider and withdraw these rejections.

Rejections under 35 USC 112, second paragraph - definiteness

The Examiner rejected claims 1, 3, 8-11, and 14 under 35 USC 112, second paragraph as allegedly being indefinite.

With respect to claim 1, Applicant submits that the claim as amended is clear. In particular, the presence of thiaminase around a cell reduces the level of thiamin. The reduced thiamin level can then induce apoptosis. Also, thiaminase "derivatives" were described in application 09/113,596 and related PCT application PCT/US98/14496, which were incorporated by reference.

With respect to claim 3, the term "contacting has its usual meaning, such that the specified bacteria are caused to be in close proximity to the cells. Thus, in claim 3 as amended, the

Claims 8 and 9 were cancelled, thereby obviating the Examiner's rejections of those claims.

Claims 10 and 11 were amended. Applicant submits that the rejections are inapplicable to claims 10 and 11 as amended.

Claim 14 was cancelled, thereby obviating the Examiner's rejections of that claim.

In view of the comments and amendments above, Applicant respectfully requests that the Examiner reconsider and withdraw the rejections for indefiniteness.

Applicant submits that the present application is now in condition for allowance, and respectfully requests notice to that effect.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Applicant hereby petitions for a two-month extension of time to make this response timely. Kindly charge the fee (Small Entity) for that extension to Deposit Account 50-0872. No additional fee is believed due in connection with this communication. However, if any additional fee is due, kindly charge the appropriate amount to Deposit Account 50-0872.

Respectfully submitted,

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APPENDIX 1: MARKED UP VERSION OF AMENDED CLAIMS SHOWING CHANGES
MADE

1. (Amended) A method of inducing apoptosis of a selected group of vertebrate cells *in vivo*, comprising administering to a vertebrate comprising said cells a thiaminase or derivative thereof or a non-pathogenic bacterium comprising a recombinant nucleic acid molecule encoding [a] said thiaminase or derivative targeted to said selected group of vertebrate cells, thereby reducing the level of thiamin in said cells sufficiently to induce apoptosis of said cells.

3. (Amended) A method for delivering [a nucleic acid sequence encoding] a thiaminase or derivative thereof to vertebrate cells *in vivo*, comprising the step of contacting said cells with a [vector] non-pathogenic bacterium comprising [said] a nucleic acid sequence encoding said thiaminase or derivative.

10. (Amended) A eukaryotic expression vector comprising a recombinant nucleic acid sequence encoding a thiaminase [of claim 9].

11. (Amended) A vector comprising a recombinant nucleic acid sequence encoding a thiaminase [of claim 9], wherein said thiaminase or derivative is different from a thiaminase from *Bacillus thiaminolyticus*.